

PATENT
Attorney Docket No. 705480
Client Reference No. 00324

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Number 6,777,231
Issued: August 17, 2004
Name of Patentee: Katz et al.
Title of Invention: ADIPOSE-DERIVED STEM CELLS AND LATTICES

**REQUEST FOR CERTIFICATE OF CORRECTION IN LIGHT OF COURT ORDER
(35 U.S.C. § 256)**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Attention: Certificates of Corrections Branch

Dear Sir:

Pursuant to 35 U.S.C. § 256, on June 9, 2008, the U.S. District Court for the Central District of California ordered correction of the inventorship for the above-referenced patent. A copy of the U.S. District Court's judgment was submitted to the USPTO on June 20, 2008, and a courtesy copy is attached hereto. Also attached is a copy of the affirmance by the U.S. Court of Appeals for the Federal Circuit, dated July 23, 2009, and which has been published at 573 F.3d 1290 (Fed. Cir. 2009).


The U.S. District Court's judgment states that "The United States Patent & Trademark Office shall correct the inventorship of the '231 patent to reflect that the correct inventors are Adam J. Katz and Ramon Llull." In view of this order, 35 U.S.C. § 256 mandates that the USPTO "Director shall issue a certificate accordingly."

Pursuant to 37 C.F.R. §§ 1.323 and/or 1.324, on behalf of University of Pittsburgh of the Commonwealth System of Higher Education, such certificate is respectfully requested. In view of the court decisions, no further factual showing is believed necessary. See MPEP 1481.02.

A proposed Certificate of Correction is attached deleting erroneously named co-inventors Futrell, Hedrick, Benhaim, Lorenz and Zhu. It will leave as co-inventors only Adam J. Katz and Ramon Llull.

The Commissioner is authorized to charge the fee of \$100 under 37 C.F.R. § 1.120(a) or, as appropriate, the fee of \$130 under 37 C.F.R. § 1.20(b), as well as any additional fee that may be deemed due to deposit account 12-1216.

Respectfully submitted,


M. Daniel Hefner, Reg. No. 41,826
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6731
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

Date: August 30, 2010

**UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION**

PATENT NO. : 6,777,231

DATED : August 17, 2004

INVENTOR(S) : Katz et al.

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

ON THE FRONT PAGE:

At (75) Inventors: Please delete the names of the following individuals: "William J. Futrell, Pittsburgh, PA (US); Marc H. Hedrick, Encino, CA (US); Prosper Benhaim, Los Angeles, CA (US); Hermann Peter Lorenz, Los Angeles, CA (US); Min Zhu, Los Angeles, CA (US)".

Inventors should read --Adam J. Katz, Charlottesville, VA (US); Ramon Llull, Mallorca (ES)--.

MAILING ADDRESS OF SENDER:

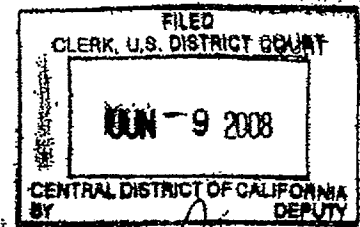
M. Daniel Hefner, Reg. No. 41,826
Leydig, Voit & Mayer, Ltd.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6731

PATENT NO. 6,777,231

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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

UNIVERSITY OF PITTSBURG OF
THE COMMONWEALTH SYSTEM
OF HIGHER EDUCATION,

Plaintiff,

v.

MARC H. HEDRICK, PROSPER
BENHAIM, HERMANN PETER
LORENZ, and MIN ZHU,

Defendants.

No. CV04-9014 CBM (AJWx)

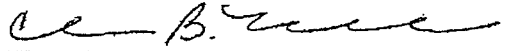
JUDGEMENT

The matter before the Court, the Honorable Consuelo B. Marshall, United States District Judge presiding, is the bench trial held on Plaintiff's claim that Defendants are not proper inventors of the United States Patent No. 6,777,231. Consistent with the Findings of Fact and Conclusions of Law issued herewith, IT IS ORDERED AND ADJUDGED that judgment be entered in favor of Plaintiffs and against Defendants. The United States Patent & Trademark Office shall correct the

1 inventorship of the '231 patent to reflect that the correct inventors are Adam J. Katz
2 and Ramon Llull.

3 **IT IS SO ORDERED.**

4 DATE: June 9, 2008



CONSUELO B. MARSHALL
UNITED STATES DISTRICT JUDGE

United States Court of Appeals for the Federal Circuit

2008-1468

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CLERK U.S. DISTRICT COURT
CENTRAL DIST. OF CALIF.
LOS ANGELES

UNIVERSITY OF PITTSBURGH
OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION,
DR. ADAM J. KATZ, and DR. RAMON LLULL,

Plaintiffs-Appellees,

v.

MARC H. HEDRICK, PROSPER BENHAIM,
HERMANN PETER LORENZ, and MIN ZHU,

Defendants-Appellants.

Judgment

ON APPEAL from the United States District Court
for the Central District of California

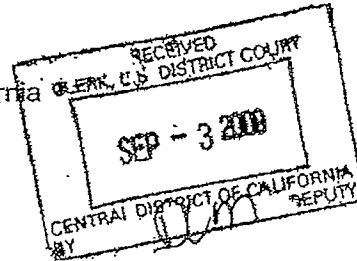
in CASE NO(S).

04-CV-9014.-CBM(ASW)

This CAUSE having been heard and considered, it is

ORDERED and ADJUDGED:

AFFIRMED



ENTERED BY ORDER OF THE COURT

DATED JUL 23 2009

Jan Horbaly, Clerk

Issued as Mandate: AUG 3 1 2009

COSTS:

Printing..... \$ 389.36

Total..... \$ 389.30

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UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

By: [Signature] Date: 8/31/09

United States Court of Appeals for the Federal Circuit

2008-1468

UNIVERSITY OF PITTSBURGH
OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION,
DR. ADAM J. KATZ, and DR. RAMON LLULL,

Plaintiffs-Appellees,

v.

MARC H. HEDRICK, PROSPER BENHAIM,
HERMANN PETER LORENZ, and MIN ZHU,

Defendants-Appellants.

Glenn J. Pfadenhauer, Williams & Connolly LLP, of Washington, DC, argued for plaintiffs-appellees. With him on the brief were Adam L. Perlman and David I. Berl.

John Allcock, DLA Piper LLP (US), of San Diego, California, argued for defendants-appellants. With him on the brief was Stanley J. Panikowski.

Appealed from: United States District Court for the Central District of California

Senior Judge Consuelo B. Marshall

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

2008-1488

UNIVERSITY OF PITTSBURGH
OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION,
DR. ADAM J. KATZ, and DR. RAMON LLULL,

Plaintiffs-Appellees,

v.

MARC H. HEDRICK, PROSPER BENHAIM,
HERMANN PETER LORENZ, and MIN ZHU,

Defendants-Appellants.

Appeal from the United States District Court for the Central District of California in case no. 04-CV-9014, Senior Judge Consuelo B. Marshall.

DECIDED: July 23, 2009

Before MAYER, RADER, and BRYSON, Circuit Judges.

MAYER, Circuit Judge.

Marc H. Hedrick, Prosper Benhaim, Hermann Peter Lorenz, and Min Zhu appeal the judgment of the United States District Court for the Central District of California finding that they were not co-inventors of U.S. Patent No. 6,777,231, and granting a misjoinder motion pursuant to 35 U.S.C. § 256. Univ. of Pittsburgh v. Hedrick, No. 2:04-cv-09014 (C.D. Cal. June 9, 2008). Because we agree that University of Pittsburgh researchers Adam Katz and Ramon Llull completed conception of the claimed invention before the appealing researchers contributed their efforts, we affirm.

BACKGROUND

Cells of the human body are generally tasked to perform specific functions. For instance, bone cells support the body, and nerve cells transmit signals throughout the body. These cells may divide and multiply to grow or heal, but a cell's progeny will usually remain of the same type as its parent cell—bone cells divide into more bone cells, nerve cells divide into more nerve cells. This feature is called unipotency, and a cell that divides to produce progeny is a progenitor cell. However, the more primitive stem cell is pluripotent, meaning that its progeny may be of various types of cells – a single stem cell may produce progeny that include both bone cells and nerve cells, for example. The process of a generic stem cell producing progeny cells of a particular type is referred to as differentiation. Generally, a cell that is the product of differentiation is permanently locked into being a progenitor of only that type of cell. Stem cells also exhibit the quality of producing further stem cells, just as a normal cell would produce a like cell through division. In a process called self-renewal, a stem cell cured in an appropriate culture dish would reproduce enough to cover the surface of the dish with like stem cells. A scientist could then remove cells and place them on a new culture dish where the process would repeat, producing a new lot of stem cells covering the surface of the dish. Each iteration is termed a passage, and it was known in the art in 1997 that stem cells can be passaged at least fifteen times without differentiating.

Katz and Lull are researchers at the University of Pittsburgh ("Pittsburgh") studying adipose (fat) tissue in humans. In 1996, the two doctors began a project at Pittsburgh involving the isolation, culturing, and passaging of cells from human liposuctioned adipose tissue. They observed that under certain conditions, mature fat

cells called adipocytes would transform into a more primitive cell having a fibroblast-like appearance, and under other circumstances, these primitive cells could transform back to mature adipocytes. They referred to these phenomena as de-differentiation and re-differentiation. By late 1996, they had developed a method to isolate these de-differentiated cells from liposuctioned tissue's stromal vascular fraction.

By 1997, Katz and Lull had explored the idea that these cells could "transdifferentiate" into lineages other than adipocyte cells, including bone, cartilage, and muscle. They recorded their observations, including that their cells appeared to change to the shape and form of non-adipose cells, contemporaneously in laboratory notebooks, a January 1997 invention disclosure for their cell isolator device, and a document titled "What's So Great About Fat?" in February 1997. Reading literature from Arnold Caplan, another researcher in stem cells, they began to recognize that the mesenchymal stem cells Caplan was harvesting from bone marrow bore similarities to those they had isolated from adipose tissue. Caplan's cells differentiated into bone, muscle, fat, and cartilage lineages, among others, and showed the ability to be passaged fifteen times without differentiating.

On January 20 and 24, and February 6, 1997, Katz wrote in his laboratory notebook that he had experimented with media to induce his cells to differentiate into muscle. In other entries, Katz described media and protocols that differentiated the cells into bone, muscle, fat, cartilage, and nerve cells. While not scientifically certain, he and Lull believed that they had observed cells changing into cells resembling muscle and fat cells, and commented to another colleague via email their intrigue over seeing "several forms that do resemble those of a neuron." They decided to do further studies

to substantiate that this was in fact a nerve cell, asking their colleague for the use of his electrophysiological techniques. By April 1997, they had the firm and definite idea that the cells were human, could be genetically modified, secreted hormones, and contained cell-surface bound intracellular signaling moieties, all properties known at the time to scientists in the field.

In July of 1997, Hedrick joined the Pittsburgh laboratory for a yearlong fellowship. During his time in the lab, Katz submitted a grant proposal summarizing his work with Llull, stating that their "lab has developed techniques to harvest, isolate, culture, passage, dedifferentiate, differentiate, and genetically alter" adipose-derived progenitor cells efficiently. While some researchers other than Katz and Llull were listed in the proposal, Hedrick was not. Hedrick was also not mentioned in Katz's laboratory notebook in connection with any work on adipose-derived stem cells, though other researchers involved in the work were mentioned. Hedrick, however, wrote his own research proposal setting forth some experiments on Katz's cells. In April of 1998, Katz, Llull, and Hedrick submitted an invention disclosure to Pittsburgh stating that the isolated cells could be induced to transform into fat, bone, cartilage, and muscle tissues, and listed the first date of conception as October 1996.

In June of 1998, Hedrick's fellowship ended, and he returned to UCLA where he formed the Regenerative Bioengineering and Research ("REBAR") laboratory with Benhaim and Lorenz. There, Hedrick and his colleagues worked on the same populations of adipose-derived cells as Katz and Llull were using at Pittsburgh. Zhu would join the lab in June 1999. The REBAR researchers determined that the adipose-derived cells were distinct from the prior art bone marrow-derived mesenchymal stem

cells because they responded differently to induction media. They also identified various media to induce differentiation in the cells, and identified the presence of an enzyme that is indicative of stem cells in a heterogeneous stromal vascular fraction population. In late 1999 and early 2000, the REBAR lab successfully cloned single adipose-derived cells. Meanwhile, Katz continued to research the exploitable potential of his cells at Pittsburgh.

In March 1999, Pittsburgh filed a provisional patent application, claiming a method of differentiating adipose-derived stem cells into bone, fat, cartilage, and muscle. The application listed Katz, Llull, William Futrell, and Hedrick as inventors. In October 1999, they filed a second provisional patent application listing the same inventors, acknowledging ongoing experimentation to find the cells in human liposuctioned fat tissue and the similarities to bone marrow-derived mesenchymal stem cells.

In February 2000, Hedrick submitted an invention disclosure to UCLA for stem cells derived from adipose tissue, listing 1997 as the date of first conception and his first successful test. Although he had not conducted any nerve differentiation experiments, he also asked the UCLA technology transfer office to include nerve cells in the patent application. About the same time, he provided Pittsburgh's patent counsel with information to include in a patent application, including recipes for induction media and the suggestion to include nerve cells.

In March 2000, Pittsburgh filed an international patent application listing all seven named inventors, Katz, Llull, Futrell, Hedrick, Benhaim, Lorenz, and Zhu. This patent

would issue as U.S. Patent No. 6,777,231 ("231 patent"), having the following 10 claims:

1. An isolated adipose-derived stem cell that can differentiate into two or more of the group consisting of a bone cell, a cartilage cell, a nerve cell, or a muscle cell.
2. An isolated, adipose-derived multipotent cell that differentiates into cells of two or more mesodermal phenotypes.
3. An isolated adipose-derived stem cell that differentiates into two or more of the group consisting of a fat cell, a bone cell, a cartilage cell, a nerve cell, or a muscle cell.
4. An isolated adipose-derived stem cell that differentiates into a combination of any of a fat cell, a bone cell, a cartilage cell, a nerve cell, or a muscle cell.
5. A substantially homogeneous population of adipose-derived stem cells, comprising a plurality of the stem cell of claim 1, 3 or 4.
6. The adipose-derived stem cell of claim 1, 3 or 4 which can be cultured for at least 15 passages without differentiating.
7. The adipose-derived stem cell of claim 1, 3 or 4 which is human.
8. The cell of any of claim 1, 3 or 4 which is genetically modified.
9. The cell of any of claim 1, 3 or 4, which has a cell-surface bound intercellular signaling moiety.
10. The cell of any of claim 1, 3 or 4, which secretes a hormone.

On October 29, 2004, Pittsburgh filed the instant action seeking the removal of named inventors Futrell, Hedrick, Benhaim, Lorenz, and Zhu. Futrell voluntarily dismissed himself from the suit leaving the REBAR researchers as the only defendants. The district court held a hearing to construe the patent claims. Among the constructions disputed was the term "adipose-derived," as is present in each claim. The REBAR researchers argued that the construction should be limited to a "species of stem cell distinct from the mesenchymal stem cell that is obtainable from bone marrow tissue" while Katz and Lull argued for a plain meaning: cells "derived from fat tissue." The court determined that the specification supports the plain meaning, and there was no disavowal of any other meaning in prosecution. So it adopted the definition proffered by Katz and Lull.

The district court then found that Katz and Lull had conceived the claimed invention as construed prior to Hedrick's arrival at Pittsburgh. In addition to the background set out above, the court supported its holding by finding that Katz and Lull must have conceived that the cells they possessed were pluripotent by February 1997, because there was no reason for Katz to have conducted his experiment attempting to induce his adipose-derived cells into non-adipose muscle cells except to confirm that the cells were in fact pluripotent stem cells. The court also found that Katz's laboratory notebooks would have enabled a scientist skilled in the field to isolate his adipose-derived cells and differentiate them into each of the lineages claimed in the '231 patent.

The REBAR researchers appeal the construction of "adipose-derived", and the conclusion that they were not joint inventors of the claimed invention. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

Claim construction is a question of law that we review de novo. Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1454-55 (Fed. Cir. 1998) (en banc). When not clearly defined in the specification, claim terms are given the meaning they would have to one of ordinary skill in the art at the time of the invention. Phillips v. AWH Corp., 415 F.3d 1303, 1312-13 (Fed. Cir. 2005). "[T]he specification is the single best guide to the meaning of a disputed term," and we read the claim terms in view of the specification. Id. at 1321 (internal quotations removed). The specification may impart a definition that differs from a term's ordinary meaning only when it demonstrates "an intent to deviate from" that meaning. Voda v. Cordis Corp., 536 F.3d 1311, 1320 (Fed. Cir. 2008) (citations omitted). Prosecution history may not be used to limit the scope of a claim

unless the applicant took a position before the Patent Office that would lead a competitor to believe that the applicant had disavowed coverage of the relevant subject matter. Schwing GmbH v. Putzmeister AG, 305 F.3d 1318, 1324-25 (Fed. Cir. 2002). Such a disavowing statement must be so clear as to show reasonable clarity and deliberateness. Omega Eng'g, Inc. v. Raytek Corp., 334 F.3d 1314, 1325 (Fed. Cir. 2003).

The district court found that one of ordinary skill would interpret the term "adipose-derived" to mean simply "derived from fat tissue." The REBAR researchers do not disagree that this is the term's plain meaning, but argue that the construction must also include that the stem cell is "a species of stem cell distinct from the mesenchymal stem cell ('MSC') that is obtainable from bone marrow tissue." This construction is necessary for their claim of inventorship because they alleged that their research proved that the inventive stem cells were in fact distinct from the prior art mesenchymal stem cells. They posit that the district court's construction would allow inclusion of prior art mesenchymal stem cells that traveled from the bone marrow and became lodged in fat tissue, where they are then extracted. They also argue that the specification makes clear that the inventive aspect of the adipose-derived stem cells is not that they are simply recovered from adipose tissue.

The REBAR researchers contend that the specification describes the prior art mesenchymal stem cells in one way, and describes the inventive adipose-derived cells differently, as an improvement upon the mesenchymal stem cells. The district court found that the specification distinguishes between mesenchymal stem cells and adipose-derived stem cells. While the specification says that the mesenchymal stem

cells require costly prescreening of culture materials, the inventive cells can be passaged in culture in an undifferentiated state not requiring prescreened lots of serum. Compare '231 Patent col.1 ll.35-39 with id. col.2 ll.16-18 and col.16 ll.1-4. However, the specification does not say that the cells are a separate species from mesenchymal stem cells collected from bone marrow as the REBAR researchers argue, just that those derived from bone marrow have different isolation requirements than those derived from adipose tissue. The court cannot impute a reason for the difference in isolation requirements of cells harvested from bone marrow versus those harvested from adipose tissue by requiring them to be of a separate species. Nor can we conclude that the hypothetical bone marrow originating stem cell that traversed and became lodged in adipose tissue would not lose the qualities that make it more difficult to isolate than its adipose-derived neighbors. That other similar prior art cells are described differently than the inventive cells does not rise to an intent to deviate from the meaning of the terms describing the inventive cells. Voda, 536 F.3d at 1320.

We similarly do not find the REBAR researchers' prosecution history argument persuasive. A patentee may limit the meaning of a claim term by making a clear and unmistakable disavowal of scope during prosecution. Purdue Pharma L.P. v. Endo Pharms., Inc., 438 F.3d 1123, 1136 (Fed. Cir. 2006). The researchers argue that Katz and Lull clearly and unambiguously disclaimed any construction of adipose-derived that could read on prior-art mesenchymal stem cells when they overcame a rejection of claims by introducing the term adipose-derived. They argue that at an interview recorded in a summary, Katz and Lull "agreed that a submission to distinguish between adipose derived stem cell and bone marrow derived stem cell will be submitted." The

subsequent submission was a paper by a UCLA group that included REBAR researchers showing that the mesenchymal stem cells and the inventive stem cells differed in their intrinsic properties. The examiner then agreed with the inventors that the "adipose-derived stem cells are distinct from the mesenchymal stem cells" of the prior art, but also noted that the claims were "now in condition for allowance" without requiring an amendment. This is not a disavowal. The examiner's summary is certainly terse, and its terseness does not allow a definition of any claim terms. It does not state why the adipose-derived stem cells in the invention are distinct from mesenchymal stem cells, and thus does not explicitly characterize the invention at all, let alone in a specific manner to overcome prior art. See Purdue Pharma, 438 F.3d at 1136. A wide chasm exists between the weak inference from the summary that adipose-derived stem cells in this invention must be a different species from mesenchymal stem cells and a clear and unmistakable disavowal as required to limit a claim term.

Inventorship is a question of law that we review de novo, based on underlying facts which we review for clear error. Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1376 (Fed. Cir. 1986). A joint invention is the product of collaboration between two or more persons working together to solve the problem addressed. 35 U.S.C. § 116 (2006). The inventors need not work physically together or contemporaneously to be joint inventors; nor must each inventor contribute equally or to each claim of the patent. Id. The inventors named in an issued patent are presumed correct, and a party alleging misjoinder of inventors must prove its case by clear and convincing evidence. Eli Lilly & Co. v. Aradigm Corp., 376 F.3d 1352, 1358 (Fed. Cir.

2004). The movants must also show that the persons to be removed did not contribute to the invention of any of the allowed claims.

Conception is the touchstone of inventorship under 35 U.S.C. § 116. It is "the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice." Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1228 (Fed. Cir. 1994) (quoting Hybritech, 802 F.2d at 1376). The test for conception is whether the inventor had an idea that was definite and permanent enough that one skilled in the art could understand the invention; the inventor must prove his conception by corroborating evidence, preferably by showing contemporaneous disclosures. Burroughs, 40 F.3d at 1228. Such corroborating evidence is taken as a whole; conception of an entire invention need not be reflected in a single source. Price v. Symsek, 988 F.2d 1188, 1196 (Fed. Cir. 1993). An inventor need not know that his invention will work for conception to be complete. Id. He need only show that he had the complete mental picture and could describe it with particularity; the discovery that the invention actually works is part of its reduction to practice. Id. In a joint invention, each inventor must contribute to the joint arrival at a definite and permanent idea of the invention as it will be used in practice. Id. at 1229.

The district court correctly applied this law, finding clear and convincing evidence that Katz and Lull conceived of each claim of the invention through contemporaneous corroboration before the arrival of Hedrick at Pittsburgh in July 1997. It found that they had recorded that their cells could transdifferentiate into multiple mesodermal lineages including bone, cartilage, fat and muscle in laboratory notebooks, letters, a January

1997 invention disclosure for their Auto-Cell Separator, the February 1997 document "What's So Great About Fat?," and the inference that Katz would have only conducted his muscle induction experiment on the cells to confirm his belief that they could differentiate into muscle instead of adipocytes. They had recorded that their isolated cells transdifferentiated into cells resembling a nerve cell in April 1997, as was recorded in a letter to a colleague requesting his help with electrophysiological techniques. While not scientifically certain that they were observing a nerve cell, they did have the firm and definite idea that nerve cells were present, and ordered further confirming tests. Claims 1, 2, 3, and 4 require an isolated adipose-derived stem cell that can differentiate into two or more mesodermal phenotypes, including specifically a fat cell, a bone cell, a cartilage cell, a nerve cell, a muscle cell, or a combination of these. Thus, the entire invention as described by claims 1, 2, 3, and 4 had been conceived and corroborated through these disclosures.

The district court found that conception of a substantially homogeneous population of the cells as required by claim 5 was satisfied by a September 1997 grant proposal describing efficiently harvesting and isolating these cells. While this writing was dated after Hedrick arrived at Pittsburgh, it does not mention Hedrick among the many other collaborators.

The district court also found that Katz and Llull grasped that their cells could self-renew as he recorded on March 20, 1997, satisfying the requirements added in claim 6. The court found that those skilled in the field at that time knew of no examples of stem cells that could not self-renew for at least 15 passages as the claim requires. Finally, the court found that Katz and Llull had the firm and definite idea that the cells were

human, could be genetically modified, secreted hormones, and contained cell-surface bound intracellular signaling moieties by April 1997 as these properties were known at the time to scientists in the field. Thus, they had conceived of the cells with the qualities required by claims 7, 8, 9, and 10, completing conception of the entire claimed invention.

The REBAR researchers do not attack these factual findings, but rather argue that Katz and Llull's research was inconclusive until Hedrick and the other researchers added their efforts. They argue that other evidence showed that Katz and Llull's work remained "highly speculative" through the end of Hedrick's fellowship. They argue that Katz and Llull were required to "know" that the invention contained every limitation of each claim at the time of conception, see Coleman v. Dines, 754 F.2d 353, 359 (Fed. Cir. 1985), but that the evidence did not establish that they had this knowledge until the REBAR researchers helped them confirm the claimed properties. Their argument is premised upon a misapprehension of what it means to "know" the limitations of the claims.

Knowledge in the context of a possessed, isolated biological construct does not mean proof to a scientific certainty that the construct is exactly what a scientist believes it is. Conception requires a definite and permanent idea of the operative invention, Burroughs, 40 F.3d at 1230, and "necessarily turns on the inventor's ability to describe his invention." Id. at 1228. Proof that the invention works to a scientific certainty is reduction to practice. Therefore, because the district court found evidence that Katz and Llull had formed a definite and permanent idea of the cells' inventive qualities, and had in fact observed them, it is immaterial that their knowledge was not scientifically

certain and that the REBAR researchers helped them gain such scientific certainty. "The determinative inquiry is not whether [the inventor's] disclosure was phrased certainly or tentatively, but whether the idea expressed therein was sufficiently developed to support conception of the subject matter." In re Jolley, 308 F.3d 1317, 1324 (Fed. Cir. 2002). The district court found that Katz's laboratory notebooks sufficiently described to those skilled in the art how to isolate the cells from adipose tissue, at which point they would be in possession of the invention. Thus, they had disclosed a "completed thought expressed in such clear terms as to enable those skilled in the art to make the invention." Coleman, 754 F.2d at 359.


The REBAR researchers also argue that the district court erred by filling in holes in Katz and Lull's conception with knowledge that a skilled artisan would have had at the time when no corroborating evidence of their own knowledge was produced. We do not find clear error in using such evidence as corroboration. "Under the 'rule of reason' standard for corroborating evidence, . . . the trial court must consider corroborating evidence in context, make necessary credibility determinations, and assign appropriate probative weight to the evidence to determine whether clear and convincing evidence supports a claim of co-inventorship." Ethicon, Inc. v. U.S. Surgical Corp., 135 F.3d 1456, 1464 (Fed. Cir. 1998) (internal citations omitted). Evidence need not always expressly show possession of the invention to corroborate conception, and a court may properly weigh evidence that a claimed attribute is merely an obvious property of a greater discovery at issue. Burroughs, 40 F.3d at 1231. Here, the greater discovery is that stem cells can be derived from adipose tissue. It was not improper for the district court to recognize that skilled artisans at the time of the alleged conception would have

known the obvious properties that these stem cells self-renew for at least 15 passages as in claim 6, that the cells contain cell-surface bound intracellular signaling moieties for claim 9, and secreted hormones for claim 10, and to credit Katz with having the firm and definite idea that these properties existed in his cells.

CONCLUSION

Accordingly, the judgment of the United States District Court for the Central District of California is affirmed.

AFFIRMED

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UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT
By:  Date: 8/31/09

stead, because the report did not state that the veteran's disability was likely service connected, and because "there was substantial evidence showing that [the veteran's disability] did not begin until after he left military service," we stated that the report was "insufficient to establish service connection."⁴ *Id.* at 1298.

CONCLUSION

For the foregoing reasons, we find no error in the Veterans Court's interpretation of 38 U.S.C. § 5107(b). To the extent Mr. Fagan argues that there is insufficient evidence supporting the denial of his claim, he presents an issue beyond our jurisdiction. *See, e.g., Maxson*, 230 F.3d at 1333 ("The weighing of this evidence is not within our appellate jurisdiction."). The decision of the Veterans Court is affirmed.

COSTS Each party shall bear its own costs.

AFFIRMED



4. However, we note—as we did in *Hogan*—that it is “troubling” to refer to statements as “non-evidence.” *Hogan*, 544 F.3d at 1297 (“the opinion of the Veterans Court contains some troubling language”). Reiterating what we said in *Hogan*, “[a] determination regarding service connection requires consideration of ‘all pertinent medical and lay evidence.’” *Id.* at 1298 (quoting 38 C.F.R. § 3.303(a)). Regardless of whether an ultimate opinion is

**UNIVERSITY OF PITTSBURGH OF
the COMMONWEALTH SYSTEM OF
HIGHER EDUCATION, Dr. Adam J.
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v.

**Marc H. HEDRICK, Prosper Benhaim,
Hermann Peter Lorenz, and Min
Zhu, Defendants–Appellants.**

No. 2008–1468.

United States Court of Appeals,
Federal Circuit.

July 23, 2009.

Background: University filed action seeking removal of independent researchers as named co-inventors with university researchers of patent involving stem cells derived from adipose tissue. The United States District Court for the Central District of California, Consuelo B. Marshall, Senior District Judge, 2007 WL 6201688, construed claims, determined that independent researchers were not co-inventors with university researchers, and granted university's misjoinder of inventors motion. Researchers appealed.

Holdings: The Court of Appeals, Mayer, Circuit Judge, held that:

- (1) adipose-derived in patent meant derived from fat tissue, and
- (2) independent researchers were not co-inventors as they contributed efforts

offered in a medical examiner's report, that report, as well as the facts discussed therein, “regarding the etiology of a claimant's [disability] must be considered as ‘evidence’ of whether the [disability] was incurred in service.” *Id.* As explained above, in this case, the Veterans Court neither adopted a restricted view of “evidence” in § 5107(b) nor failed to consider any pertinent evidence.

after university researchers completed conception of patent.

Affirmed.

1. Patents \S 324.5

Patent claim construction is a question of law reviewed de novo.

2. Patents \S 161

When not clearly defined in the specification, patent claim terms are given the meaning they would have to one of ordinary skill in the art at the time of the invention.

3. Patents \S 167(1)

The specification is the single best guide to the meaning of a disputed patent claim term, and the claim terms are read in view of the specification.

4. Patents \S 167(1.1)

The specification may impart a definition that differs from a patent claim term's ordinary meaning only when it demonstrates an intent to deviate from that meaning.

5. Patents \S 168(2.1)

Prosecution history may not be used to limit the scope of a patent claim unless the applicant took a position before the Patent and Trademark Office that would lead a competitor to believe that the applicant had disavowed coverage of the relevant subject matter; such a disavowing statement must be so clear as to show reasonable clarity and deliberateness.

6. Patents \S 101(2)

"Adipose-derived" in patent involving stem cells derived from adipose tissue meant derived from fat tissue.

7. Patents \S 168(2.1)

A patentee may limit the meaning of a claim term by making a clear and unmistakable disavowal of scope during prosecution.

8. Patents \S 168(3)

Patent examiner's summary providing weak inference that adipose-derived stem cells in claimed invention were different species from mesenchymal stem cells did not constitute unmistakable disavowal of scope during prosecution, as required to limit meaning of claim term, since summary's terseness did not allow definition of any claim terms, did not state why adipose-derived stem cells in invention were distinct from mesenchymal stem cells, and thus did not explicitly characterize invention at all, let alone in specific manner to overcome prior art.

9. Patents \S 324.5, 324.55(2)

Inventorship is a question of law reviewed de novo, based on underlying facts which are reviewed for clear error.

10. Patents \S 112.1, 112.5

The inventors named in an issued patent are presumed correct, and a party alleging misjoinder of inventors must prove its case by clear and convincing evidence and must also show that the persons to be removed did not contribute to the invention of any of the allowed claims.

11. Patents \S 90(1)

"Conception" is the touchstone of inventorship and is the formation in the mind of the inventor of a definite and permanent idea of the complete and operative invention as it is hereafter to be applied in practice. 35 U.S.C.A. § 116.

See publication Words and Phrases for other judicial constructions and definitions.

12. Patents \S 90(1), 91(3)

The test for conception is whether the inventor had an idea that was sufficiently definite and permanent that one skilled in the art could understand the invention; the inventor must prove his conception by corroborating evidence, preferably by

showing contemporaneous disclosures. 35 U.S.C.A. § 116.

13. Patents ⇨91(3)

An inventor's corroborating evidence to prove conception is taken as a whole; conception of an entire invention need not be reflected in a single source. 35 U.S.C.A. § 116.

14. Patents ⇨90(1, 5)

An inventor need not know that his invention will work for conception to be complete, rather, he need only show that he had the complete mental picture and could describe it with particularity; the discovery that the invention actually works is part of its reduction to practice. 35 U.S.C.A. § 116.

15. Patents ⇨92

In a joint invention, each inventor must contribute to the joint arrival at a definite and permanent idea of the invention as it will be used in practice. 35 U.S.C.A. § 116.

16. Patents ⇨92

University researchers conceived of each claim of invention, involving stem cells derived from adipose tissue, and corroborated each claim through contemporaneous disclosures prior to independent researchers contributing their efforts, as required for removal of independent researchers as named joint inventors of patent, since university researchers' laboratory notebooks sufficiently described to those skilled in art how to isolate cells from adipose tissue, at which point researchers were in possession of invention based on their disclosure of completed thought expressed with particularity. 35 U.S.C.A. § 116.

17. Patents ⇨91(4)

"Knowledge" of limitation of patent claims in the context of a possessed, isolated biological construct does not mean proof to a scientific certainty that the con-

struct is exactly what a scientist believes it is.

See publication Words and Phrases for other judicial constructions and definitions.

18. Patents ⇨90(1)

Conception requires a definite and permanent idea of the operative invention, and necessarily turns on the inventor's ability to describe his invention. 35 U.S.C.A. § 116.

19. Patents ⇨90(5)

Proof that the invention works to a scientific certainty is reduction to practice.

20. Patents ⇨90(1)

The determinative conception inquiry is not whether the inventor's disclosure was phrased certainly or tentatively, but whether the idea expressed therein was sufficiently developed to support conception of the subject matter. 35 U.S.C.A. § 116.

21. Patents ⇨91(3)

Under the rule of reason standard for corroborating evidence of conception, the trial court must consider corroborating evidence in context, make necessary credibility determinations, and assign appropriate probative weight to the evidence to determine whether clear and convincing evidence supports a claim of co-inventorship. 35 U.S.C.A. § 116.

22. Patents ⇨91(3)

Evidence need not always expressly show possession of the invention to corroborate conception, and the trial court may properly weigh evidence that a claimed attribute is merely an obvious property of a greater discovery at issue. 35 U.S.C.A. § 116.

Patents ⇨328(2)

6,777,231. Construed.

Glenn J. Pfadenhauer, Williams & Connolly LLP, of Washington, DC, argued for plaintiffs-appellees. With him on the brief were Adam L. Perlman and David I. Berl.

John Allcock, DLA Piper LLP (US), of San Diego, CA, argued for defendants-appellants. With him on the brief was Stanley J. Panikowski.

Before MAYER, RADER, and BRYSON, Circuit Judges.

MAYER, Circuit Judge.

Marc H. Hedrick, Prosper Benhaim, Hermann Peter Lorenz, and Min Zhu appeal the judgment of the United States District Court for the Central District of California finding that they were not co-inventors of U.S. Patent No. 6,777,231, and granting a misjoinder motion pursuant to 35 U.S.C. § 256. *Univ. of Pittsburgh v. Hedrick*, No. 2:04-cv-09014 (C.D. Cal. June 9, 2008). Because we agree that University of Pittsburgh researchers Adam Katz and Ramon Llull completed conception of the claimed invention before the appealing researchers contributed their efforts, we affirm.

BACKGROUND

Cells of the human body are generally tasked to perform specific functions. For instance, bone cells support the body, and nerve cells transmit signals throughout the body. These cells may divide and multiply to grow or heal, but a cell's progeny will usually remain of the same type as its parent cell—bone cells divide into more bone cells, nerve cells divide into more nerve cells. This feature is called unipotency, and a cell that divides to produce progeny is a progenitor cell. However, the more primitive stem cell is pluripotent, meaning that its progeny may be of various types of cells—a single stem cell may produce progeny that include both bone cells and nerve cells, for example. The process of a generic stem cell producing

progeny cells of a particular type is referred to as differentiation. Generally, a cell that is the product of differentiation is permanently locked into being a progenitor of only that type of cell. Stem cells also exhibit the quality of producing further stem cells, just as a normal cell would produce a like cell through division. In a process called self-renewal, a stem cell cured in an appropriate culture dish would reproduce enough to cover the surface of the dish with like stem cells. A scientist could then remove cells and place them on a new culture dish where the process would repeat, producing a new lot of stem cells covering the surface of the dish. Each iteration is termed a passage, and it was known in the art in 1997 that stem cells can be passaged at least fifteen times without differentiating.

Katz and Llull are researchers at the University of Pittsburgh ("Pittsburgh") studying adipose (fat) tissue in humans. In 1996, the two doctors began a project at Pittsburgh involving the isolation, culturing, and passaging of cells from human liposuctioned adipose tissue. They observed that under certain conditions, mature fat cells called adipocytes would transform into a more primitive cell having a fibroblast-like appearance, and under other circumstances, these primitive cells could transform back to mature adipocytes. They referred to these phenomena as de-differentiation and re-differentiation. By late 1996, they had developed a method to isolate these dedifferentiated cells from liposuctioned tissue's stromal vascular fraction.

By 1997, Katz and Llull had explored the idea that these cells could "transdifferentiate" into lineages other than adipocyte cells, including bone, cartilage, and muscle. They recorded their observations, including that their cells appeared to change to the shape and form of non-adipose cells,

contemporaneously in laboratory notebooks, a January 1997 invention disclosure for their cell isolator device, and a document titled "What's So Great About Fat?" in February 1997. Reading literature from Arnold Caplan, another researcher in stem cells, they began to recognize that the mesenchymal stem cells Caplan was harvesting from bone marrow bore similarities to those they had isolated from adipose tissue. Caplan's cells differentiated into bone, muscle, fat, and cartilage lineages, among others, and showed the ability to be passaged fifteen times without differentiating.

On January 20 and 24, and February 6, 1997, Katz wrote in his laboratory notebook that he had experimented with media to induce his cells to differentiate into muscle. In other entries, Katz described media and protocols that differentiated the cells into bone, muscle, fat, cartilage, and nerve cells. While not scientifically certain, he and Llull believed that they had observed cells changing into cells resembling muscle and fat cells, and commented to another colleague via email their intrigue over seeing "several forms that do resemble those of a neuron." They decided to do further studies to substantiate that this was in fact a nerve cell, asking their colleague for the use of his electrophysiological techniques. By April 1997, they had the firm and definite idea that the cells were human, could be genetically modified, secreted hormones, and contained cell-surface bound intracellular signaling moieties, all properties known at the time to scientists in the field.

In July of 1997, Hedrick joined the Pittsburgh laboratory for a yearlong fellowship. During his time in the lab, Katz submitted a grant proposal summarizing his work with Llull, stating that their "lab has developed techniques to harvest, isolate, culture, passage, dedifferentiate, differentiate, and genetically alter" adipose-

derived progenitor cells efficiently. While some researchers other than Katz and Llull were listed in the proposal, Hedrick was not. Hedrick was also not mentioned in Katz's laboratory notebook in connection with any work on adipose-derived stem cells, though other researchers involved in the work were mentioned. Hedrick, however, wrote his own research proposal setting forth some experiments on Katz's cells. In April of 1998, Katz, Llull, and Hedrick submitted an invention disclosure to Pittsburgh stating that the isolated cells could be induced to transform into fat, bone, cartilage, and muscle tissues, and listed the first date of conception as October 1996.

In June of 1998, Hedrick's fellowship ended, and he returned to UCLA where he formed the Regenerative Bioengineering and Research ("REBAR") laboratory with Benhaim and Lorenz. There, Hedrick and his colleagues worked on the same populations of adipose-derived cells as Katz and Llull were using at Pittsburgh. Zhu would join the lab in June 1999. The REBAR researchers determined that the adipose-derived cells were distinct from the prior art bone marrow-derived mesenchymal stem cells because they responded differently to induction media. They also identified various media to induce differentiation in the cells, and identified the presence of an enzyme that is indicative of stem cells in a heterogeneous stromal vascular fraction population. In late 1999 and early 2000, the REBAR lab successfully cloned single adipose-derived cells. Meanwhile, Katz continued to research the exploitable potential of his cells at Pittsburgh.

In March 1999, Pittsburgh filed a provisional patent application, claiming a method of differentiating adipose-derived stem cells into bone, fat, cartilage, and muscle. The application listed Katz, Llull, William Futrell, and Hedrick as inventors. In Oc-

tober 1999, they filed a second provisional patent application listing the same inventors, acknowledging ongoing experimentation to find the cells in human liposuctioned fat tissue and the similarities to bone marrow-derived mesenchymal stem cells.

In February 2000, Hedrick submitted an invention disclosure to UCLA for stem cells derived from adipose tissue, listing 1997 as the date of first conception and his first successful test. Although he had not conducted any nerve differentiation experiments, he also asked the UCLA technology transfer office to include nerve cells in the patent application. About the same time, he provided Pittsburgh's patent counsel with information to include in a patent application, including recipes for induction media and the suggestion to include nerve cells.

In March 2000, Pittsburgh filed an international patent application listing all seven named inventors, Katz, Llull, Futrell, Hedrick, Benhaim, Lorenz, and Zhu. This patent would issue as U.S. Patent No. 6,777,231 ("231 patent"), having the following 10 claims:

1. An isolated adipose-derived stem cell that can differentiate into two or more of the group consisting of a bone cell, a cartilage cell, a nerve cell, or a muscle cell.
2. An isolated, adipose-derived multipotent cell that differentiates into cells of two or more mesodermal phenotypes.
3. An isolated adipose-derived stem cell that differentiates into two or more of the group consisting of a fat cell, a bone cell, a cartilage cell, a nerve cell, or a muscle cell.
4. An isolated adipose-derived stem cell that differentiates into a combination of any of a fat cell, a bone cell, a cartilage cell, a nerve cell, or a muscle cell.

5. A substantially homogeneous population of adipose-derived stem cells, comprising a plurality of the stem cell of claim 1, 3 or 4.
6. The adipose-derived stem cell of claim 1, 3 or 4 which can be cultured for at least 15 passages without differentiating.
7. The adipose-derived stem cell of claim 1, 3 or 4 which is human.
8. The cell of any of claim 1, 3 or 4 which is genetically modified.
9. The cell of any of claim 1, 3 or 4, which has a cell-surface bound intercellular signaling moiety.
10. The cell of any of claim 1, 3 or 4, which secretes a hormone.

On October 29, 2004, Pittsburgh filed the instant action seeking the removal of named inventors Futrell, Hedrick, Benhaim, Lorenz, and Zhu. Futrell voluntarily dismissed himself from the suit leaving the REBAR researchers as the only defendants. The district court held a hearing to construe the patent claims. Among the constructions disputed was the term "adipose-derived," as is present in each claim. The REBAR researchers argued that the construction should be limited to a "species of stem cell distinct from the mesenchymal stem cell that is obtainable from bone marrow tissue" while Katz and Llull argued for a plain meaning: cells "derived from fat tissue." The court determined that the specification supports the plain meaning, and there was no disavowal of any other meaning in prosecution. So it adopted the definition proffered by Katz and Llull.

The district court then found that Katz and Llull had conceived the claimed invention as construed prior to Hedrick's arrival at Pittsburgh. In addition to the background set out above, the court supported its holding by finding that Katz and Llull must have conceived that the cells they

possessed were pluripotent by February 1997, because there was no reason for Katz to have conducted his experiment attempting to induce his adipose-derived cells into non-adipose muscle cells except to confirm that the cells were in fact pluripotent stem cells. The court also found that Katz's laboratory notebooks would have enabled a scientist skilled in the field to isolate his adipose-derived cells and differentiate them into each of the lineages claimed in the '231 patent.

The REBAR researchers appeal the construction of "adipose-derived", and the conclusion that they were not joint inventors of the claimed invention. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

[1-5] Claim construction is a question of law that we review *de novo*. *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1454-55 (Fed.Cir.1998) (en banc). When not clearly defined in the specification, claim terms are given the meaning they would have to one of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed.Cir.2005). "[T]he specification is the single best guide to the meaning of a disputed term," and we read the claim terms in view of the specification. *Id.* at 1321 (internal quotations removed). The specification may impart a definition that differs from a term's ordinary meaning only when it demonstrates "an intent to deviate from" that meaning. *Voda v. Cordis Corp.*, 536 F.3d 1311, 1320 (Fed.Cir.2008) (citations omitted). Prosecution history may not be used to limit the scope of a claim unless the applicant took a position before the Patent Office that would lead a competitor to believe that the applicant had disavowed coverage of the relevant subject matter. *Schwing GmbH v. Putzmeister Aktiengesellschaft and Putzmeister*, 305 F.3d 1318, 1324-25 (Fed.Cir.2002).

Such a disavowing statement must be so clear as to show reasonable clarity and deliberateness. *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1325 (Fed. Cir.2003).

[6] The district court found that one of ordinary skill would interpret the term "adipose-derived" to mean simply "derived from fat tissue." The REBAR researchers do not disagree that this is the term's plain meaning, but argue that the construction must also include that the stem cell is "a species of stem cell distinct from the mesenchymal stem cell ('MSC') that is obtainable from bone marrow tissue." This construction is necessary for their claim of inventorship because they alleged that their research proved that the inventive stem cells were in fact distinct from the prior art mesenchymal stem cells. They posit that the district court's construction would allow inclusion of prior art mesenchymal stem cells that traveled from the bone marrow and became lodged in fat tissue, where they are then extracted. They also argue that the specification makes clear that the inventive aspect of the adipose-derived stem cells is not that they are simply recovered from adipose tissue.

The REBAR researchers contend that the specification describes the prior art mesenchymal stem cells in one way, and describes the inventive adipose-derived cells differently, as an improvement upon the mesenchymal stem cells. The district court found that the specification distinguishes between mesenchymal stem cells and adipose-derived stem cells. While the specification says that the mesenchymal stem cells require costly prescreening of culture materials, the inventive cells can be passaged in culture in an undifferentiated state not requiring prescreened lots of serum. Compare '231 Patent col.1 ll.35-39 with *id.* col.2 ll.16-18 and col. 16 ll.1-4.

However, the specification does not say that the cells are a separate species from mesenchymal stem cells collected from bone marrow as the REBAR researchers argue, just that those derived from bone marrow have different isolation requirements than those derived from adipose tissue. The court cannot impute a reason for the difference in isolation requirements of cells harvested from bone marrow versus those harvested from adipose tissue by requiring them to be of a separate species. Nor can we conclude that the hypothetical bone marrow originating stem cell that traversed and became lodged in adipose tissue would not lose the qualities that make it more difficult to isolate than its adipose-derived neighbors. That other similar prior art cells are described differently than the inventive cells does not rise to an intent to deviate from the meaning of the terms describing the inventive cells. *Voda*, 536 F.3d at 1320.

[7, 8] We similarly do not find the REBAR researchers' prosecution history argument persuasive. A patentee may limit the meaning of a claim term by making a clear and unmistakable disavowal of scope during prosecution. *Purdue Pharma L.P. v. Endo Pharms., Inc.*, 438 F.3d 1123, 1136 (Fed.Cir.2006). The researchers argue that Katz and Llull clearly and unambiguously disclaimed any construction of adipose-derived that could read on prior-art mesenchymal stem cells when they overcame a rejection of claims by introducing the term adipose-derived. They argue that at an interview recorded in a summary, Katz and Llull "agreed that a submission to distinguish between adipose derived stem cell and bone marrow derived stem cell will be submitted." The subsequent submission was a paper by a UCLA group that included REBAR researchers showing that the mesenchymal stem cells and the inventive stem cells differed in their intrinsic properties. The examiner then agreed with the inventors that the

"adipose-derived stem cells are distinct from the mesenchymal stem cells" of the prior art, but also noted that the claims were "now in condition for allowance" without requiring an amendment. This is not a disavowal. The examiner's summary is certainly terse, and its terseness does not allow a definition of any claim terms. It does not state why the adipose-derived stem cells in the invention are distinct from mesenchymal stem cells, and thus does not explicitly characterize the invention at all, let alone in a specific manner to overcome prior art. *See Purdue Pharma*, 438 F.3d at 1136. A wide chasm exists between the weak inference from the summary that adipose-derived stem cells in this invention must be a different species from mesenchymal stem cells and a clear and unmistakable disavowal as required to limit a claim term.

[9, 10] Inventorship is a question of law that we review *de novo*, based on underlying facts which we review for clear error. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1376 (Fed.Cir. 1986). A joint invention is the product of collaboration between two or more persons working together to solve the problem addressed. 35 U.S.C. § 116 (2006). The inventors need not work physically together or contemporaneously to be joint inventors; nor must each inventor contribute equally or to each claim of the patent. *Id.* The inventors named in an issued patent are presumed correct, and a party alleging misjoinder of inventors must prove its case by clear and convincing evidence. *Eli Lilly & Co. v. Aradigm Corp.*, 376 F.3d 1352, 1358 (Fed.Cir.2004). The movants must also show that the persons to be removed did not contribute to the invention of any of the allowed claims.

[11–15] Conception is the touchstone of inventorship under 35 U.S.C. § 116. It is "the formation in the mind of the inventor,

of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice." *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1228 (Fed.Cir.1994) (quoting *Hybritech*, 802 F.2d at 1376). The test for conception is whether the inventor had an idea that was definite and permanent enough that one skilled in the art could understand the invention; the inventor must prove his conception by corroborating evidence, preferably by showing contemporaneous disclosures. *Burroughs*, 40 F.3d at 1228. Such corroborating evidence is taken as a whole; conception of an entire invention need not be reflected in a single source. *Price v. Symsek*, 988 F.2d 1187, 1196 (Fed.Cir.1993). An inventor need not know that his invention will work for conception to be complete. *Id.* He need only show that he had the complete mental picture and could describe it with particularity; the discovery that the invention actually works is part of its reduction to practice. *Id.* In a joint invention, each inventor must contribute to the joint arrival at a definite and permanent idea of the invention as it will be used in practice. *Id.* at 1229.

[16] The district court correctly applied this law, finding clear and convincing evidence that Katz and Lull conceived of each claim of the invention through contemporaneous corroboration before the arrival of Hedrick at Pittsburgh in July 1997. It found that they had recorded that their cells could transdifferentiate into multiple mesodermal lineages including bone, cartilage, fat and muscle in laboratory notebooks, letters, a January 1997 invention disclosure for their Auto-Cell Separator, the February 1997 document "What's So Great About Fat?," and the inference that Katz would have only conducted his muscle induction experiment on the cells to confirm his belief that they could differentiate into muscle instead of adipocytes. They had recorded that their isolated cells

transdifferentiated into cells resembling a nerve cell in April 1997, as was recorded in a letter to a colleague requesting his help with electrophysiological techniques. While not scientifically certain that they were observing a nerve cell, they did have the firm and definite idea that nerve cells were present, and ordered further confirming tests. Claims 1, 2, 3, and 4 require an isolated adipose-derived stem cell that can differentiate into two or more mesodermal phenotypes, including specifically a fat cell, a bone cell, a cartilage cell, a nerve cell, a muscle cell, or a combination of these. Thus, the entire invention as described by claims 1, 2, 3, and 4 had been conceived and corroborated through these disclosures.

The district court found that conception of a substantially homogeneous population of the cells as required by claim 5 was satisfied by a September 1997 grant proposal describing efficiently harvesting and isolating these cells. While this writing was dated after Hedrick arrived at Pittsburgh, it does not mention Hedrick among the many other collaborators.

The district court also found that Katz and Lull grasped that their cells could self-renew as he recorded on March 20, 1997, satisfying the requirements added in claim 6. The court found that those skilled in the field at that time knew of no examples of stem cells that could not self-renew for at least 15 passages as the claim requires. Finally, the court found that Katz and Lull had the firm and definite idea that the cells were human, could be genetically modified, secreted hormones, and contained cell-surface bound intracellular signaling moieties by April 1997 as these properties were known at the time to scientists in the field. Thus, they had conceived of the cells with the qualities required by claims 7, 8, 9, and 10, completing conception of the entire claimed invention.

The REBAR researchers do not attack these factual findings, but rather argue that Katz and Llull's research was inconclusive until Hedrick and the other researchers added their efforts. They argue that other evidence showed that Katz and Llull's work remained "highly speculative" through the end of Hedrick's fellowship. They argue that Katz and Llull were required to "know" that the invention contained every limitation of each claim at the time of conception, see *Coleman v. Dines*, 754 F.2d 353, 359 (Fed.Cir.1985), but that the evidence did not establish that they had this knowledge until the REBAR researchers helped them confirm the claimed properties. Their argument is premised upon a misapprehension of what it means to "know" the limitations of the claims.

[17–20] Knowledge in the context of a possessed, isolated biological construct does not mean proof to a scientific certainty that the construct is exactly what a scientist believes it is. Conception requires a definite and permanent idea of the operative invention, *Burroughs*, 40 F.3d at 1230, and "necessarily turns on the inventor's ability to describe his invention." *Id.* at 1228. Proof that the invention works to a scientific certainty is reduction to practice. Therefore, because the district court found evidence that Katz and Llull had formed a definite and permanent idea of the cells' inventive qualities, and had in fact observed them, it is immaterial that their knowledge was not scientifically certain and that the REBAR researchers helped them gain such scientific certainty. "The determinative inquiry is not whether [the inventor's] disclosure was phrased certainly or tentatively, but whether the idea expressed therein was sufficiently developed to support conception of the subject matter." *In re Jolley*, 308 F.3d 1317, 1324 (Fed.Cir.2002). The district court found that Katz's laboratory notebooks sufficiently described to those skilled in the art how to isolate the cells from adi-

pose-tissue, at which point they would be in possession of the invention. Thus, they had disclosed a "completed thought expressed in such clear terms as to enable those skilled in the art to make the invention." *Coleman*, 754 F.2d at 359.

[21, 22] The REBAR researchers also argue that the district court erred by filling in holes in Katz and Llull's conception with knowledge that a skilled artisan would have had at the time when no corroborating evidence of their own knowledge was produced. We do not find clear error in using such evidence as corroboration. "Under the 'rule of reason' standard for corroborating evidence, . . . the trial court must consider corroborating evidence in context, make necessary credibility determinations, and assign appropriate probative weight to the evidence to determine whether clear and convincing evidence supports a claim of co-inventorship." *Ethicon, Inc. v. U.S. Surgical Corp.*, 135 F.3d 1456, 1464 (Fed.Cir.1998) (internal citations omitted). Evidence need not always expressly show possession of the invention to corroborate conception, and a court may properly weigh evidence that a claimed attribute is merely an obvious property of a greater discovery at issue. *Burroughs*, 40 F.3d at 1231. Here, the greater discovery is that stem cells can be derived from adipose tissue. It was not improper for the district court to recognize that skilled artisans at the time of the alleged conception would have known the obvious properties that these stem cells self-renew for at least 15 passages as in claim 6, that the cells contain cell-surface bound intracellular signaling moieties for claim 9, and secreted hormones for claim 10, and to credit Katz with having the firm and definite idea that these properties existed in his cells.

CONCLUSION

Accordingly, the judgment of the United States District Court for the Central District of California is affirmed.

AFFIRMED



In re **HOTELS.COM, L.P.**

No. 2008-1429.

No. 78/277,681.

United States Court of Appeals,
Federal Circuit.

July 23, 2009.

Background: Operator of online hotel reservation service appealed decision of the United States Patent and Trademark Office, Trademark Trial and Appeal Board (TTAB), 2008 WL 779325, refusing to register service mark **HOTELS.COM**, on ground that mark was generic term for such services.

Holding: The Court of Appeals, Newman, Circuit Judge, held that TTAB's determination was supported by substantial evidence.

Affirmed.

1. Trademarks ⇌1689

Whether particular term is generic, and therefore cannot be trademark or service mark, is question of fact.

2. Trademarks ⇌1308, 1310

Patent and Trademark Office (PTO) bears burden of establishing that proposed mark is generic, and must demonstrate generic status by clear evidence.

3. Trademarks ⇌1322

Court of Appeals gives plenary review to legal conclusions of Trademark Trial and Appeal Board (TTAB), and reviews its factual findings to determine whether they

are arbitrary, capricious, or unsupported by substantial evidence.

4. Trademarks ⇌1322

On appellate review of Trademark Trial and Appeal Board's (TTAB) factual finding of genericness, Court of Appeals determines whether, on entirety of the record, there was substantial evidence to support the determination.

5. Trademarks ⇌1322

When fact is required to be found by "clear evidence" and not mere preponderance, review of findings of Trademark Trial and Appeal Board (TTAB) for support by substantial evidence must take this heightened burden into account.

6. Trademarks ⇌1034

Generic term cannot be registered as trademark, for generic terms by definition are incapable of indicating source.

7. Trademarks ⇌1037

Term that is descriptive, but not generic, may acquire distinctiveness and serve as trademark.

8. Trademarks ⇌1044, 1058

Finding by Trademark Trial and Appeal Board (TTAB) that proposed service mark **HOTELS.COM** was generic term for hotel information and reservations, and could not be registered, was supported by substantial evidence; terms "hotel" and ".com" in combination had meaning identical to common meaning of separate components.

9. Trademarks ⇌1619

In trademark dispute, survey evidence is subject to review for its probative value, based on factors including design of survey, questions asked, and experience of surveyor.

Trademarks ⇌1800

HOTELS.COM.